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(71) Applicant (*for all designated States except US*): **EVOTEC NEUROSCIENCES GMBH** [DE/DE]; Schnackenburgallee 114, 22525 Hamburg (DE).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **HIPFEL, Rainer** [DE/DE]; Albert-Fränkel-Str. 6, 69126 Heidelberg (DE). **VON DER KAMMER, Heinz** [DE/DE]; Verbindungsstr. 6d, 22607 Hamburg (DE). **POHLNER, Johannes** [DE/DE]; Quittenweg 11, 22175 Hamburg (DE).

(74) Agents: **MEYERS, Hans-Wilhelm** et al.; P.O. Box 10 22 41, 50462 Cologne (DE).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **DIAGNOSTIC AND THERAPEUTIC USE OF THE VOLTAGE-GATED ION CHANNEL SCN2A FOR NEURODEGENERATIVE DISEASES**

(57) Abstract: The present invention discloses the differential expression of the gene coding for the voltage-gated ion channel SCN2A in specific brain regions of Alzheimer's disease patients. Based on this finding, this invention provides a method for diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, in a subject, or for determining whether a subject is at increased risk of developing such a disease. Furthermore, this invention provides therapeutic and prophylactic methods for treating or preventing Alzheimer's disease and related neurodegenerative disorders using the voltage-gated ion channel gene SCN2A and its corresponding gene products. A method of screening for modulating agents of neurodegenerative diseases is also disclosed.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/00400

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 A01K67/027 A61K49/00 C07K16/28 C07K14/705
A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N A01K A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PLANELLIS-CASES R ET AL: "Neuronal death and perinatal lethality in voltage-gated sodium channel alpha(II)-deficient mice." BIOPHYSICAL JOURNAL. UNITED STATES JUN 2000, vol. 78, no. 6, June 2000 (2000-06), pages 2878-2891, XP008006212 ISSN: 0006-3495	18-22, 30-32
Y	cited in the application the whole document --- -/--	1-11

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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- *A* document defining the general state of the art which is not considered to be of particular relevance
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Date of international completion of the international search

9 May 2003

Date of mailing of the international search report

28/05/2003

Mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel: (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Schalich, J

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/00400

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KEARNEY J A ET AL: "A gain-of-function mutation in the sodium channel gene Scn2a results in seizures and behavioral abnormalities." NEUROSCIENCE. UNITED STATES 2001, vol. 102, no. 2, 2001, pages 307-317, XP002208817 ISSN: 0306-4522 cited in the application	18-22, 30,31
Y	the whole document	1-11
X	WO 01 38564 A (LAFRENIERE RONALD G ;ROULEAU GUY A (CA); UNIV MCGILL (CA); RAGSDAL) 31 May 2001 (2001-05-31)	23,24
Y	page 40, line 16 -page 43, line 29	1-11

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 12-17, 25-29

Present claims 12-17 and 25-29 relate to compounds and their use defined by reference to a desirable characteristic or property, namely to modulate a level or an activity of the gene and/or the corresponding protein SCN2A.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for no such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no search -which goes beyond saxitoxin and tetrodotoxin, 2 inhibitors of sodium channels well-known to persons skilled in the art- has been carried out for claims:

12-17, 25-29

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/00400

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 12
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☒ Claims Nos.: 12-17, 25-29
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/00400

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0138564	A	31-05-2001	AU	1846501 A		04-06-2001
			WO	0138564 A2		31-05-2001
			CA	2394229 A1		31-05-2001
			EP	1252330 A2		30-10-2002
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